

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Previously Presented) An isolated infectious recombinant respiratory syncytial virus (RSV) comprising a major nucleocapsid (N) protein, a nucleocapsid phosphoprotein (P), a large polymerase protein (L), a M2(ORF1) RNA polymerase elongation factor, and a partial or complete recombinant RSV genome or antigenome having one or more shifted RSV gene(s) or genome segment(s) within said recombinant genome or antigenome that is/are positionally shifted to a more promoter-proximal or promoter-distal position relative to a position of said RSV gene(s) or genome segment(s) within a wild type RSV genome or antigenome.

2. (Original) The isolated infectious recombinant RSV of claim 1, wherein said one or more shifted gene(s) or genome segment(s) is/are shifted to a more promoter-proximal or promoter-distal position by deletion or insertion of one or more displacement polynucleotide(s) within said partial or complete recombinant RSV genome or antigenome.

3. (Original) The isolated infectious recombinant RSV of claim 2, wherein said displacement polynucleotide(s) comprise(s) one or more polynucleotide insert(s) of between 150 nucleotides (nts) and 4,000 nucleotides in length which is inserted in a non-coding region (NCR) of the genome or antigenome or as a separate gene unit (GU), said polynucleotide insert lacking a complete open reading frame (ORF) and specifying an attenuated phenotype in said recombinant RSV.

4. (Original) The isolated infectious recombinant RSV of claim 3, wherein said polynucleotide insert(s) comprises one or more RSV gene(s) or genome segment(s).

5. (Original) The isolated infectious recombinant RSV of claim 2, wherein said displacement polynucleotide(s) comprise(s) one or more RSV gene(s) or genome segment(s) selected from RSV NS1, NS2, N, P, M, SH, M2(ORF1), M2(ORF2), L, F and

G genes and genome segments and leader, trailer and intergenic regions of the RSV genome and segments thereof.

6. (Original) The isolated infectious recombinant RSV of claim 2, wherein said displacement polynucleotide(s) comprise(s) one or more bovine RSV (BRSV) or human RSV (HRSV) gene(s) or genome segment(s) selected from RSV NS1, NS2, N, P, M, SH, M2(ORF1), M2(ORF2), L, F and G gene(s) or genome segment(s) and leader, trailer and intergenic regions of the RSV genome or segments thereof.

7. (Original) The isolated infectious recombinant RSV of claim 6, wherein said displacement polynucleotide(s) is/are deleted to form the recombinant RSV genome or antigenome to cause a positional shift of said one or more shifted RSV gene(s) or genome segment(s) within said recombinant genome or antigenome to a more promoter-proximal position relative to a position of said RSV gene(s) or genome segment(s) within a wild type RSV genome or antigenome.

8. (Original) The isolated infectious recombinant RSV of claim 7, wherein said displacement polynucleotide(s) that is/are deleted to form the recombinant RSV genome or antigenome comprise one or more RSV NS1, NS2, SH, M2(ORF2), or G gene(s) or genome segment(s) thereof.

9. (Original) The isolated infectious recombinant RSV of claim 8, wherein a displacement polynucleotide comprising a RSV NS1 gene is deleted to form the recombinant RSV genome or antigenome.

10. (Original) The isolated infectious recombinant RSV of claim 8, wherein a displacement polynucleotide comprising a RSV NS2 gene is deleted to form the recombinant RSV genome or antigenome.

11. (Original) The isolated infectious recombinant RSV of claim 8, wherein a displacement polynucleotide comprising a RSV SH gene is deleted to form the recombinant RSV genome or antigenome.

12. (Original) The isolated infectious recombinant RSV of claim 8, wherein a displacement polynucleotide comprising RSV M2(ORF2) is deleted to form the recombinant RSV genome or antigenome.

13. (Original) The isolated infectious recombinant RSV of claim 8, wherein a displacement polynucleotide comprising a RSV G gene is deleted to form the recombinant RSV genome or antigenome or antigenome.

14. (Original) The isolated infectious recombinant RSV of claim 8, wherein the RSV F and G genes are both deleted to form the recombinant RSV genome or antigenome or antigenome.

15. (Original) The isolated infectious recombinant RSV of claim 8, wherein the RSV NS1 and NS2 genes are both deleted to form the recombinant RSV genome or antigenome or antigenome.

16. (Original) The isolated infectious recombinant RSV of claim 8, wherein the RSV SH and NS2 genes are both deleted to form the recombinant RSV genome or antigenome or antigenome.

17. (Original) The isolated infectious recombinant RSV of claim 8, wherein the RSV SH, NS1 and NS2 genes are all deleted to form the recombinant RSV genome or antigenome or antigenome.

18. (Original) The isolated infectious recombinant RSV of claim 7, wherein said displacement polynucleotide(s) comprise(s) one or more deletion(s) within a nontranslated sequence at the beginning or end of an RSV open reading frame or in an intergenic region or 3' leader or 5' trailer portion of the RSV genome.

19. (Original) The isolated infectious recombinant RSV of claim 18, wherein said displacement polynucleotides comprise a partial gene deletion.

20. (Original) The isolated infectious recombinant RSV of claim 19, wherein said partial gene deletion is a partial deletion of the SH gene.

21. (Original) The isolated infectious recombinant RSV of claim 20, wherein said partial deletion of the SH gene comprises a deletion within the SH downstream non-translated region.

22. (Original) The isolated infectious recombinant RSV of claim 21, which is RSV 6120 having a deletion of 112 nucleotides at positions 4499-4610 in the recombinant RSV antigenome.

23. (Original) The isolated infectious recombinant RSV of claim 7, wherein said displacement polynucleotide(s) is/are selected from one or more region(s) of a downstream untranslated sequence of an RSV gene.

24. (Original) The isolated infectious recombinant RSV of claim 23, wherein said downstream untranslated sequence(s) is/are from NS1 (positions 519-563), NS2 (positions 1003-1086), P (positions 3073-3230), M (positions 4033-4197), F(positions 7387-7539), and/or M2 (positions 8433-8490) genes.

25. (Original) The isolated infectious recombinant RSV of claim 7, wherein said displacement polynucleotide(s) is/are selected from one or more region(s) of a upstream untranslated sequence of an RSV gene.

26. (Original) The isolated infectious recombinant RSV of claim 25, wherein said one or more upstream untranslated sequences is/are from NS1 (positions 55-96), NS2 (positions 606-624) and/or SH (positions 4231-4300).

27. (Original) The isolated infectious recombinant RSV of claim 7, wherein said displacement polynucleotide comprises a deletion of nucleotides 4683 to 4685 of the RSV G gene.

28. (Original) The isolated infectious recombinant RSV of claim 7, wherein said displacement polynucleotide(s) is/are selected from one or more RSV intergenic sequences.

29. (Original) The isolated infectious recombinant RSV of claim 7, wherein said displacement polynucleotide(s) is/are selected from nucleotides within the RSV 5' trailer region.

30. (Original) The isolated infectious recombinant RSV of claim 29, wherein a portion of the 5' trailer region that immediately follows the L gene is reduced in size by 75 nucleotides, 100 nucleotides, 125 nucleotides, or more, leaving intact the 5' genomic terminus.

31. (Original) The isolated infectious recombinant RSV of claim 7, wherein said displacement polynucleotide(s) is/are selected from nucleotides within the RSV 3' leader region.

32. (Original) The isolated infectious recombinant RSV of claim 31, wherein a portion of the 3' trailer region that excludes a core portion of the viral promoter located within the first 11 nucleotides of the 3' leader is deleted.

33. (Original) The isolated infectious recombinant RSV of claim 7, wherein a partial or complete deletion from one or any combination of the RSV NS1, NS2, SH, F and/or M2 genes yields an adjustable reduction in genome length of between 1-806 nucleotides.

34. (Original) The isolated infectious recombinant RSV of claim 7, wherein a partial or complete deletion from one or any combination of RSV intergenic regions yields an adjustable reduction in genome length of between 1-198 nucleotides.

35. (Original) The isolated infectious recombinant RSV of claim 7, wherein a partial or complete deletion from one or any combination of RSV intergenic regions yields an adjustable reduction in genome length of between 1-198 nucleotides.

36. (Original) The isolated infectious recombinant RSV of claim 6, wherein said displacement polynucleotide(s) is/are added, substituted, or rearranged within the recombinant RSV genome or antigenome to cause a positional shift of said one or more shifted RSV gene(s) or genome segment(s) within said recombinant genome or antigenome to a more promoter-proximal or promoter-distal position relative to a position of said RSV gene(s) or genome segment(s) within a wild type RSV genome or antigenome.

37. (Original) The isolated infectious recombinant RSV of claim 36, wherein said displacement polynucleotide(s) added, substituted, or rearranged within the recombinant RSV genome or antigenome comprise(s) one or more RSV NS1, NS2, SH, M2(ORF2), F, and/or G gene(s) or genome segment(s) thereof.

38. (Original) The isolated infectious recombinant RSV of claim 36, wherein said displacement polynucleotide(s) comprise(s) one or more RSV gene(s) or genome segment(s) encoding one or more RSV glycoprotein(s) or immunogenic domain(s) or epitope(s) thereof.

39. (Original) The isolated infectious recombinant RSV of claim 38, wherein said displacement polynucleotide(s) is/are selected from gene(s) or genome segment(s) encoding RSV F, G, and/or SH glycoprotein(s) or immunogenic domain(s) or epitope(s) thereof.

40. (Original) The isolated infectious recombinant RSV of claim 1, wherein one or more RSV glycoprotein gene(s) or genome segments of RSV F, G and SH is/are added, substituted or rearranged within said recombinant RSV genome or antigenome to a position that is more promoter-proximal compared to a wild type gene order position of said one or more RSV glycoprotein gene(s).

41. (Original) The isolated infectious recombinant RSV of claim 40, wherein the RSV glycoprotein gene G is rearranged within said recombinant RSV genome or antigenome to a gene order position that is more promoter-proximal compared to the wild type gene order position of G.

42. (Original) The isolated infectious recombinant RSV of claim 41, wherein the RSV glycoprotein gene G is shifted to gene order position 1 within said recombinant RSV genome or antigenome.

43. (Original) The isolated infectious recombinant RSV of claim 40, wherein the RSV glycoprotein gene F is rearranged within said recombinant RSV genome or antigenome to a gene order position that is more promoter-proximal compared to the wild type gene order position of F.

44. (Original) The isolated infectious recombinant RSV of claim 43, wherein the RSV glycoprotein gene F is shifted to gene order position 1 within said recombinant RSV genome or antigenome.

45. (Original) The isolated infectious recombinant RSV of claim 40, wherein both RSV glycoprotein genes G and F are rearranged within said recombinant RSV genome or antigenome to gene order positions that are more promoter-proximal compared to the wild type gene order positions of G and F.

46. (Original) The isolated infectious recombinant RSV of claim 45, wherein the RSV glycoprotein gene G is shifted to gene order position 1 and the RSV glycoprotein gene F is shifted to gene order position 2 within said recombinant RSV genome or antigenome.

47. (Original) The isolated infectious recombinant RSV of claim 40, wherein one or more RSV NS1, NS2, SH, M2(ORF2), or G gene(s) or genome segment(s) thereof is/are deleted in the recombinant RSV genome or antigenome.

48. (Original) The isolated infectious recombinant RSV of claim 40, wherein a displacement polynucleotide comprising a RSV NS1 gene is deleted to form the recombinant RSV genome or antigenome.

49. (Original) The isolated infectious recombinant RSV of claim 40, wherein a displacement polynucleotide comprising a RSV NS2 gene is deleted to form the recombinant RSV genome or antigenome.

50. (Original) The isolated infectious recombinant RSV of claim 40 wherein a displacement polynucleotide comprising a RSV SH gene is deleted to form the recombinant RSV genome or antigenome.

51. (Original) The isolated infectious recombinant RSV of claim 50, wherein the RSV glycoprotein gene G is rearranged within said recombinant RSV genome or antigenome to a gene order position that is more promoter-proximal compared to the wild type gene order position of G.

52. (Original) The isolated infectious recombinant RSV of claim 51, wherein the RSV glycoprotein gene G is shifted to gene order position 1 within said recombinant RSV genome or antigenome.

53. (Original) The isolated infectious recombinant RSV of claim 52, which is G1/ΔSH.

54. (Original) The isolated infectious recombinant RSV of claim 50, wherein the RSV glycoprotein gene F is rearranged within said recombinant RSV genome or antigenome to a gene order position that is more promoter-proximal compared to the wild type gene order position of F.

55. (Original) The isolated infectious recombinant RSV of claim 54, wherein the RSV glycoprotein gene F is shifted to gene order position 1 within said recombinant RSV genome or antigenome.

56. (Original) The isolated infectious recombinant RSV of claim 55, which is F1/ΔSH.

57. (Original) The isolated infectious recombinant RSV of claim 50, wherein both RSV glycoprotein genes G and F are rearranged within said recombinant RSV genome or antigenome to gene order positions that are more promoter-proximal compared to the wild type gene order positions of G and F.

58. (Original) The isolated infectious recombinant RSV of claim 57, wherein the RSV glycoprotein gene G is shifted to gene order position 1 and the RSV glycoprotein gene F is shifted to gene order position 2 within said recombinant RSV genome or antigenome.

59. (Original) The isolated infectious recombinant RSV of claim 58, which is G1F2/ΔSH.

60. (Original) The isolated infectious recombinant RSV of claim 40, wherein the RSV SH and NS2 genes are both deleted to form the recombinant RSV genome or antigenome or genome.

61. (Original) The isolated infectious recombinant RSV of claim 60, wherein both RSV glycoprotein genes G and F are rearranged within said recombinant RSV genome or antigenome to gene order positions that are more promoter-proximal compared to the wild type gene order positions of G and F.

62. (Original) The isolated infectious recombinant RSV of claim 61, wherein the RSV glycoprotein gene G is shifted to gene order position 1 and the RSV glycoprotein gene F is shifted to gene order position 2 within said recombinant RSV genome or antigenome.

63. (Original) The isolated infectious recombinant RSV of claim 62, which is G1F2/ΔNS2ΔSH.

64. (Original) The isolated infectious recombinant RSV of claim 40, wherein the RSV SH, NS1 and NS2 genes are all deleted to form the recombinant RSV genome or antigenome or genome.

65. (Original) The isolated infectious recombinant RSV of claim 64, wherein both RSV glycoprotein genes G and F are rearranged within said recombinant RSV genome or antigenome to gene order positions that are more promoter-proximal compared to the wild type gene order positions of G and F.

66. (Original) The isolated infectious recombinant RSV of claim 65, wherein the RSV glycoprotein gene G is shifted to gene order position 1 and the RSV glycoprotein gene F is shifted to gene order position 2 within said recombinant RSV genome or antigenome.

67. (Original) The isolated infectious recombinant RSV of claim 66, which is G1F2/ΔNS2ΔNS2ΔSH.

68-69. (Cancelled.)

70. (Previously Presented) The isolated infectious recombinant RSV of claim 1 which is a complete virus.

71. (Original) The isolated infectious recombinant RSV of claim 1 which is a subviral particle.

72. (Original) The isolated infectious recombinant RSV of claim 2, wherein said displacement polynucleotide is added within or deleted from a noncoding region of the recombinant RSV genome or antigenome.

73. (Original) The isolated infectious recombinant RSV of claim 1, wherein the recombinant genome or antigenome incorporates antigenic determinants from one or both subgroup A and subgroup B human RSV.

74. (Rejoined—Currently Amended) A method for stimulating the immune system of an individual to ~~induce protection~~ elicit an immune response against RSV which comprises administering to the individual an immunologically sufficient amount of the recombinant RSV of claim 1 combined with a physiologically acceptable carrier.

75. (Rejoined) The method of claim 100, wherein the recombinant RSV is administered in a dose of 10^3 to 10^6 PFU.

76. (Rejoined) The method of claim 100, wherein the recombinant RSV is administered to the upper respiratory tract.

77. (Rejoined) The method of claim 100, wherein the recombinant RSV is administered by spray, droplet or aerosol.

78. (Rejoined) The method of claim 100, wherein the recombinant RSV is administered to an individual seronegative for antibodies to RSV or possessing transplacentally acquired maternal antibodies to RSV.

79. (Rejoined) The method of claim 100, wherein the recombinant RSV elicits an immune response against either human RSV A or RSV B.

80. (Withdrawn) The method of claim 100, wherein the recombinant RSV elicits an immune response against both human RSV A and RSV B.

81. (Rejoined) The method of claim 100, wherein the recombinant RSV elicits an immune response against either human RSV A or RSV B and is co-administered with an immunologically sufficient amount of a second attenuated RSV capable of eliciting an immune response against human RSV A or RSV B, whereby an immune response is elicited against both human RSV A and RSV B.

82. (Rejoined) The method of claim 107, wherein the recombinant RSV and second attenuated RSV are administered simultaneously as a mixture.

83. (Original) An immunogenic composition to elicit an immune response against RSV comprising an immunologically sufficient amount of the recombinant RSV of claim 1 in a physiologically acceptable carrier.

84. (Original) The immunogenic composition of claim 109, formulated in a dose of 10^3 to 10^6 PFU.

85. (Original) The immunogenic composition of claim 109, formulated for administration to the upper respiratory tract by spray, droplet or aerosol.

86. (Original) The immunogenic composition of claim 109, wherein the recombinant RSV elicits an immune response against either human RSV A or RSV B or both human RSV A and RSV B.

87-197. (Cancelled)

88. (Rejoined-Currently Amended) A method for producing an infectious attenuated recombinant RSV particle from one or more isolated polynucleotide molecules encoding said RSV, comprising:

expressing in a cell or cell-free lysate an expression vector comprising an isolated polynucleotide comprising a recombinant RSV genome or antigenome having one or more shifted RSV gene(s) or genome segment(s) within said recombinant genome or antigenome that is/are positionally shifted to a more promoter-proximal or promoter-distal position relative to a position of said RSV gene(s) or genome segment(s) within a wild type RSV genome or antigenome, and RSV N, P, L and M2ORF1 RNA polymerase elongation factor proteins.

89. (Rejoined-Currently Amended) The method of claim 198, wherein the recombinant RSV genome or antigenome and the N, P, L and M2ORF1 RNA polymerase elongation factor proteins are expressed by two or more different expression vectors.

90-207. (Cancelled)